

# **APPLICATION FOR PATENT**

## **INVENTORS:**

**Teresa Leigh Barr**

**Stephen D. Holt**

## **TITLE: PAIN RELIEVER AND METHOD OF USE**

## **SPECIFICATION**

### **BACKGROUND OF THE INVENTION**

This is a continuation in part application of Serial No. 09/408,740 filed September 29, 1999.

In one aspect, this invention relates to a composition of matter useful for treating bodily pains and discomforts. In another aspect, this invention relates to a method for treating bodily pains and discomforts. In yet another aspect, this invention relates to formulating a pain and discomfort reliever.

Arthritis is medically termed as an inflammation of a joint or joints and is one of a number of diseases and disorders of the skeleton and body system. Arthritis arises from many causes, some well-defined, some still unknown, and it is treated in many different ways. There are two common types, the first of which is inflammatory, of which rheumatoid arthritis is the most commonly acknowledged and a non-inflammatory, second type, most commonly represented by degenerative joint disease, or wear and tear arthritis. Inflammatory arthritis is a disease not of the joints alone but of the whole bodily system, in particular, the connective tissues of the body. It is an autoimmune disease,

where the body's immune system attacks its own host (i.e. itself) and produces inflammation. Degenerative joint disease is a chronic joint disease, often occurring in more elderly people. In both cases many manifestations are similar. The joints, whether singly or in multiples, are affected. The joints may become swollen, warm, deformed, gnarled, and in many instances present grotesque deformities. In many cases it also affects the adjacent muscles and tendons, as well as other connective tissues of the body. The primary disease produces symptomatic swelling, pain and stiffness.

Various new and old drugs have been developed for the treatment of arthritis, anywhere from non-steroidal anti-inflammatory drugs to cortisone. Many of these systemic drugs have dangerous side effects. Their dosage must be carefully prescribed and administered under controlled conditions and circumstances to avoid unpleasant and dangerous side effects.

Several topical agents (creams, ointments, liniments, lotions and the like) have been utilized for the relief of the pains and aches of arthritis. Most of these have provided a little, but only temporary, relief to persons suffering from pain. Many combinations of varying ointments, creams, aqueous solutions, liniments and the like for the treatment of arthritis are known. The most efficacious of these contains as its active ingredient the vegetable products derived from the seed and pods of the capsicum plant, commonly known as red pepper. Capsicum-derived ointment is devised for external application to the affected area of the body by applying to the area adjacent to the muscle, joint or tendon and rubbing it into the skin. The active ingredient is capsaicin. With initial as well as persistent application, capsaicin is effective to relieve the aches and pains of various muscle or skeletal origin, such as arthritis, muscle strains, tendonitis, bursitis and soft tissue diseases.

Capsaicin is also effective to relieve the various musculoskeletal pains, itching, neuropathic pains, dysesthesias caused by shingles, post herpetic neuralgia, post

mastectomy pain, and peripheral neuropathies. It is further commonly prescribed to reduce the pain of neuropathies produced by diabetes (burning pain, discomfort, often at night) and other diseases that are neuropathic in origin including the discomfort and odd sensations of shingles (post herpetic neuralgia, which can be extremely painful), as well as dysesthesias that can occur with thoracotomies and post surgical scars.

Unfortunately, although capsaicin is often the most effective agent available, the active ingredient is a potent skin irritant, producing a burning, uncomfortable sensation to the skin. Although prescribed frequently, it is used to only a limited extent due to this unpleasant side effect.

The burning side effect has also discouraged the use of capsaicin to treat other types of discomfort, such as pruritus or itching. Pruritus or itching can be caused by many stimuli, such as poison ivy, hemorrhoids, or athlete's foot. The unpleasant side effects of capsaicin have discouraged its use to treat such types of discomfort. Also, the burning that occurs when the skin is exposed to sunlight that has been treated with capsaicin or exposed to water has discouraged the use of capsaicin.

A capsaicin based pain reliever which does not irritate the skin or cause a burning discomfort even when exposed to water and sunlight, would be extremely desirable and acceptable to patients and people in general who are experiencing the types of pain or discomfort outlined above.

Prior attempts to produce such an invention can be seen in US Patent No. 5,134,166 and US Patent No. 4,997,853, which use anesthetics in association with capsaicin, effectively numbing sites. The present invention does not attempt to numb the site, but instead permits continued use of the hand or foot, with sensory input remaining in tact, rather than simply blocking all sensory input to the area while warming with capsaicin.

## OBJECTS OF THE INVENTION

It is an object of this invention to provide a capsaicin based pain reliever, which can be applied transdermally.

5

It is another object of this invention to provide a method for formulating a no-burn capsaicin-based pain reliever for tendons, muscles and joints in which the capsaicin is fully functional, one, which provides analgesic and anesthetic properties.

10 Another object of the invention is to provide a topical formulation, which can be used for blows and strains to muscles.

## SUMMARY OF THE INVENTION

15 In accordance with one aspect of the invention, there is provided a composition comprising a carrier, capsaicin, an encapsulation agent, an ester of amino acid and a light-diffusing compound.

20 In accordance with another aspect of the invention, there is provided a method for treating a victim of pain or discomfort. The treatment comprises applying the above-described composition topically to the skin of the victim near an area affected by the pain or discomfort.

25 In accordance with a further aspect of the invention, there is provided a method for making a composition useful for topical application to treat pain or discomfort. The method is carried out by mixing a carrier to form an aqueous solution, adding an encapsulation agent to reduce burning of the capsaicin, adding an amount of esters of amino acids and finally adding a light refractive element having an ability to stop secondary burning effect by the capsaicin due to the suns rays. The resulting aqueous

solution preferably has a cream-like viscosity.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

5    The present invention has been devised to use in nerve damage treatment. such as after a patient has experienced shingles. Additionally, the present invention is a composition for the treatment of the following conditions: arthritis, tendonitis, bursitis, myositis, myalgia and arthralgia.

10    Capsaicin is trans-8-methyl-N-vanillyl-5 none amide, a naturally occurring alkyl vanillylamide, a type of capsaicinoid. It is found in high concentration in fruit of plants of the Capsicum genus. The chili pepper, red pepper and paprika are all species of Capsicum. All hot papers contain capsaicinoids. Capsaicinoids are natural materials, which produce a burning sensation in the mouth. Capsicum has recently been officially  
15    defined in the USP 23 where it is defined as the dried ripe fruit of Capsicum frutescens Linne or Capsicum annum Linne.

There are two main capsaicinoids, capsaicin and dihydrocapsaicin and three minor capsaicinoids, nordihydrocapsaicin, homocapsaicin and homodihydrocapsaicin. All  
20    capsaicinoids are considered usable within the scope of this invention.

Capsicum is the dry powder obtained by grinding up the fruits of these plants. Capsicum oleoresin (or capsaicin oleoresin) is the liquid concentrate extracted from the dry powder. Capsaicin, a white crystalline material, is obtained from the liquid concentrate.

25

The composition of the invention comprises capsaicin as a first active ingredient and at least one-second active ingredient acting as an analgesic to reduce the sensation of capsaicin induced skin irritation. The ingredients are contained in a carrier fluid. The genus capsicum is a member of a large tropical family solanaceae. There are numerous

Species, of which *Capsicum annum*, *Capsicum chinense* and *Capsicum frutescens* are closely related. *Capsicum frutescens* is also known as Cayenne Pepper, Chili Pepper, Pimento Tabasco Pepper and Tabasco-sauce pepper.

- 5 Capsaicin (N-Vanillyl-8-methyl-6- (E)-nonoic amide) is the most pungent of the capsaicinoids. It is very soluble in fats, oils and alcohols. Capsicum also contains a red coloring matter, oleic acid, palmitic acid and stearic acid.

- 10 *Capsicum frutescens* extract can be obtained from Bio-Botanica, Inc. of Hauppauge, New York and appears as a viscous fluid, having a sallow yellow color, a caustic and pungent aroma, and is soluble in ethanol.

Capsicum is a powerful local stimulant. It is strongly rubefacient acting without vesication.

15

- Generally speaking, the composition will contain in the range of 0.00125% to 1% by weight of capsaicin. However, compositions containing less than 0.00125% by weight, down to 0.0001% of capsaicin will provide a therapeutic, effect. Even trace concentrations of capsaicin (such as 0.00001% by weight) will provide a minute therapeutic effect. Compositions containing more than 1% by weight of capsaicin will also provide a therapeutic effect, up to 62% by weight capsaicin, except that the burning side effect will increase in proportion to the increase percentage of capsaicin. Compositions containing 0.025% to 20% by weight of capsaicin could be used. Compositions of 0.025 to 2% by weight are considered usable as well. Even so, 25 compositions containing in the range of 0.025% to 0.25% by weight of capsaicin are preferred because they are narrowly encompassed within current FDA guidelines. However, the FDA guidelines were developed at a time when there was not an effective method for relieving the discomfort generated by capsaicin. The present invention provides a method to increase the amount of capsaicin that can be administered

comfortably.

In the present invention, capsaicin is mixed with a carrier fluid. Preferably, the carrier fluid is water-based and forms an aqueous solution containing the ingredients. However, the carrier may be a fluid such as an oil based carrier, a fat based carrier, a fatty alcohol based carrier or combination of these.

Additional irritant is added to the capsaicin and carrier. Histidines, such as a histamine dihydrochloride are considered usable in the scope of the present invention to create vasodilatation, and act as a second irritant. Adding the second irritant produces an analgesic effect and does not numb the site, like an anesthetic or depress cutaneous sensory receptors. It is possible to add more than one histidine to achieve the analgesic reaction. Instead, it has a topical counterirritant effect by stimulating cutaneous sensory receptors, see, Federal Register, Vol 48, No. 27, Tuesday February 8, 1983, pages 5367 et. seq., Specifically, amine and caine type local anesthetics, such as benzocaine and lidocaine, act differently as anesthetics not producing an analgesic effect which is achieved by adding an additional irritant, such as a histamine hydrochloride or most preferably a histamine dihydrochloride. If a histamine dihydrochloride is used, it is preferred to use a starting composition of 98% histamine, although compositions in the range of 96-99% histamine will be usable as well.

Any one of the following histidines, or combinations thereof, are considered usable in this invention, L-histidines, histamine dihydrochloride, DL-histidine, D-histidine hydrochloride monohydrate, L-histidine hydrochloride monohydrate, L-histidine methyl ester dihydrochloride, L-histidinol dihydrochloride.

When histidines are used in the invention, it is preferred that the weight percent of the material is between 0.001% and about 1.0 wt. %. However in the most preferred embodiment, 0.025 and 0.10 wt. % are contemplated.

Other histidines are considered usable within the scope of this invention, as well as the second irritant. It is possible though, that the invention will work well with out the second irritant

5

The novel composition further comprises an encapsulation agent such as colloidal oatmeal, hydrogenated lecithin, dipotassium glycyrrhizinate or other similar encapsulation agents, or even combinations of these agents with the capsaicin and second irritant. The colloidal oatmeal has intrinsic SFP, natural sunscreen capability. In addition, the colloidal oatmeal can serve to encapsulate the capsaicin to reduce the inflammation effect the capsaicin has on the skin, while still enabling the capsaicin to work effectively. Typically, 0.35 wt. % colloidal oatmeal is used in this invention, although any amount between 0.20 and up to about 0.60 wt. percent can be used. The colloidal oatmeal works within the scope of this invention because it contains hydrophilic colloids. These colloids help to provide a protective barrier on the skin to control inflammation. In addition, histidines, such as L-histidines, are present in colloid oatmeal. Histidines can be present in the oats in weight percents up to 3% of the total amino acids in the oats. The invention has found that using the colloidal oats enhance, synergistically the histamine dichlorohydrate effect, when histamine dichlorohydrate is used.

20

The dipotassium glycyrrhizinate is prepared from finely cut licorice root extracted with water. Ethanol is then added to this extract and the precipitate is separated after sedimentation. Inorganic acid is added to the filtrate, and the precipitating sediment is filtered. After neutralization with water, it is dissolved in a potassium hydroxide solution and evaporated until dry. The residue is recrystallized in media such as acetic acid or ethanol to obtain monopotassium glycyrrhizinate. The product is faintly yellow without an odor and sweet in taste. Typically this product can be acquired from Barnet Products Corp. of Englewood Cliffs, New Jersey.

25



Hydrogenated lecithin is available from Barnet Products Corporation, as well. It is an emulsifier and stabilizer for solutions. In addition, it is used to reduce inflammation on the skin. The unique lecithin will synergistically react with the dipotassium glycyrrhizinate to enhance the effect of the dipotassium glycyrrhizinate on encapsulation of the capsaicin. Additionally, the lecithin is used to reduce irritation, which differs from inflammation. Inflamed skin is red and hot, irritated skin is itchy without necessarily being inflamed and red.

Esters of amino acids are next added to the formulation. Esters of amino acid usable in the scope of this invention are preferably menthyl and lauryl esters of amino acids. In the most preferred embodiment, the esters of amino acid are menthyl lauryl pidolate. This ester is comprised of menthyl as well as pidolic acid and lauric alcohol. This component has no odor. Typically, 0.1 - 1.0 wt. % is used in this compound in order to create the necessary analgesic effect. The active element in this component is menthol, which acts as an analgesic. It is considered within the scope of the present invention to use enough menthyl lauryl pidolate to attain between 0.1 and 16 wt % menthol in the formulation.

Additionally, polysorbate and benzyl alcohol can be added to the formulation. It is contemplated that the amount added can be in weight percents based on the total formula of about 0.1 - 8% by weight. The polysorbate is believed to add the feature of a emulsifier & stabilizer. The benzyl alcohol can be added to the formulation to add the feature of keeping the skin from burning and acting as a solvent for the colloidal oats as well as a preservative.

The unique formulation is a topically (externally) applied formulation which has three simultaneous effects, analgesic, anesthetic and antipruritic effects, by (1) depressing cutaneous sensory receptors to relieve pain and (2) stimulating cutaneous sensory receptors using a topical counter irritant.

It is the combination of analgesic and anesthetic which make this invention unique.

Further, a light scattering compound is added to the formulation. Light scattering compounds can be any compounds, which have the ability to scatter light, such as by using particles having a diameter up to about 100 microns and more preferably between  
5 30-60 microns.

Titanium dioxide is considered the best light scattering element for the present invention. Titanium dioxides usable within the scope of the present invention are preferably fine particle or pigmentary titanium dioxides available from Solaveil, of Durham, England.  
10 Any of the Solavil  $\text{TiO}_2$  products for cosmetic use can be used. All will reflect ultraviolet and provide broad UVB light protection, effectively scattering the light rays. In a preferred embodiment, the  $\text{TiO}_2$  can provide a complete block of sunlight, and when mixed with the colloidal oatmeal, the light waves can be refracted and the skin protected from burning from the light.

15 Other than titanium dioxides, other components can be used for the light scattering purpose. For example, octyl dodecyl neopentanoate can be used for light scattering. Bernell Chemical sells these compounds. Zinc oxide can be used as light scattering component, which also has the advantage of being anti-itch, or anti-pruritic effect.

20 Also, benzophenones, methoxycinnamate, para amino benzoic acid and combinations thereof can be used. It is also within the scope of the present invention, to add component onto the surface of the titanium dioxide to further enhance the effect of the titanium dioxide. In particular, aluminum stearate and aluminum oxide can be  
25 additionally used with the titanium dioxide for light scattering.

The titanium dioxide, with or without the aluminum is typically dispersed in caprylic/capric triglyceride, causing this component to contain approximately 50% by weight of solids.

It should be noted that other additives may be used in the present invention such as xanthum gum, myristal myristate and other stearates for coagulation of the compound.

5 Additional components can be added to the formulation, such as "lavender flower oil" or **lavender oil**, and a "bergaptene -free" bergamot oil or bergamot extract is expected to be beneficial in that the lavender provides a muscle relaxant characteristic and the bergamot oil provides help with acne, fevers, herpes, and diabetic neuropathy.

10 Also, for enhancing the composition, other elements may be added to the composition. The following are contemplated:

1. Arnica montana
2. Hypericum perforatum (known as St. John's Wort)
- 15 3. Aloe barbadensis gel
4. Citric acid to adjust the pH of the compound
5. Propylene glycol with methyl and propyl parabens as preservatives
6. A chealating agent to keep the product from separating, such as edetatedisodium
- 20 7. Triethanolamine hydrochloride which acts as a reagent
8. Other preservatives

Still others considered usable in the present invention are phenoxy ethanol, ethyl paraben, and butyl paraben as preservatives, or in the preservative system. Other ingredients such  
25 as inositol, methyl paraben, propyl paraben, hydroxy ethyl cellulose can be used therein, for formulations which are gels rather than creams. Carbomer 940 can be used to make the formula into a gel rather than a cream.

Xanthum gum can be added to the invention to provide a higher density compound, and  
30 act as a thickening agent. Other elements, such as licorice extract, glyceryl polymethacrylate and hydroxypropyl cellulose can be used in various formulations of the basic invention.

A suspension agent can be added to the formula of the present invention. Alkyl benzoate  
35 is considered usable within the scope of the present invention, and helps to suspend the particle size of components used in this system.

Deionized water is an excellent aqueous carrier for the present invention.

5 The present invention is fast acting and long acting due to the menthol present in the compositions. The uses of the invention are contemplated for post peripetic neuralgia, and scar conditions after surgery, such as for treating the scars from a mastectomy. Also, the present invention is considered usable for victims of neuropathy, such as diabetes with neuropathy.

10 In the method of the invention, a victim of pain or discomfort is treated by applying the above-described composition topically to the skin of the victim near an area affected by the pain or discomfort. The types of pain or discomfort to which the invention may be applied include those discussed in the background of the invention. Generally speaking, the inventive composition, preferably in cream, ointment and lotion form, is applied to  
15 the selected area, such as a joint, and rubbed in. The amount applied is not critical. Generally, it should be applied in an amount that is sufficient to wet the area of application. Usually, the amount used will be in the range of from about 0.3 to about 3 cc's.

20 For the treatment of pruritus or itching, the application of the composition can be repeated as required to control the discomfort. When the preferred composition of the invention is applied, it provides near immediate relief from the itching caused by poison ivy or hemorrhoids, without a burning sensation. The relief lasts for several hours. It is surprising that a capsaicin-based composition would be useful for the treatment of such  
25 discomfort. To enhance the antipruritic effect, additional compounds can be added to the formulation. These components can be methyl sulphonyl methane, sodium bicarbonate, calamine, allantoin, kaolin, cortisone, anti-inflammatory steroids, anti-allergic steroids, and combinations or derivatives thereof.

For best results in the treatment of arthritis, the treatment should be repeated several times per day, such as in the range of 2 to 8 times per day, preferably 3-5 times per day, and continued for several days. Surprisingly, most patients do not experience the burning discomfort heretofore known as a very common side effect of topical capsaicin application.

It is contemplated to be within the scope of the present invention to use this formulation for a gel, a cream, an opaque cream, a spray using propellants, such as butyl propellants, and a liquid or lotion, such as a roll on.

10

It is even contemplated that the present invention could be used as a patch for treatment as well. Propellant for the spray on composition contemplated as usable herein can be selected from the group butane, propane, isobutane, and combinations thereof. A foam version of the formulation, additionally using a propellant and a surfactant is considered within the scope of the present invention. A preferred surfactant is a member of the group of amine oxides. The most preferred surfactant is alkyl dimethyl amine oxide.

15

The forgoing is a description of the composition and method of use of three embodiments of the invention. The scope of the invention is considered to include the described embodiment together with others obvious to those skilled in the art.

20

## COMPOSITION EXAMPLE

The resulting composition made in accordance with one embodiment of the invention contains the following ingredients.

5	<b>Ingredient</b>	<b>wt. %</b>
	deionized water	Q.S.
	triethanolamine hydrochloride	0.05
	edetate disodium	0.05
	methyl paraben	0.03
10	propyl paraben	0.02
	<b>lavender oil</b>	<b>4.0</b>
	capsaicin	0.0133
	Arnica montana extract	1.0%
	Aloe barbadensis gel	15.0%
15	colloidal oatmeal	12.0%
	hydrogenated lecithin	0.05%
	stearates	10.0%
	myristal myristate	1.0%
	polysorbate	20.0%
20	titanium dioxide solution (50% solids)	10.0%
	benzyl alcohol	8%

In addition to the above ingredients, up to 10% by weight of the formulation can be carbopol. Additionally, hydroxypropyl cellulose can be used up to 5% or hydroxymethyl  
25 cellulose can be used in up to the same amount. Also, a methyl sulfonyl methane, from 10-15% by weight of the entire formulation can be used to assist with pain in the tendons and the joints.

### Second Preferred Embodiment

In an alternative embodiment, the following elements are preferred:

- Aloe vera gel
- Amica Montana
- 5 Benzly alcohol
- Caprylic-capric triglyceride
- Titanium dioxide
- Alumina
- Polyhydroxy stearate
- 10 Lavender oil
- Cetyl alcohol
- Colloidal oatmeal
- Glyceryl monostearate
- Lecithin
- 15 Myristal myristate
- PEG 100 stearate
- Phenoxyethanol
- Methyl paraben
- Ethylparaben
- 20 Propylparaben
- Butylparaben
- Polysorbate 80
- Tetrasodium EDTA
- Triethanolimine

25

#### **Transdermal Application**

The present invention related to a composition which can be used in a form which has absorption rates which permit transdermal application to a skin and an ability to penetrate

[illegible]